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        JAN 28
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                 U.S. National Patent Classification
NEWS 14 MAR 31
                 IFICDB, IFIPAT, and IFIUDB enhanced with new custom
                 IPC display formats
NEWS 15
         MAR 31
                 CAS REGISTRY enhanced with additional experimental
NEWS 16
         MAR 31
                 CA/CAplus and CASREACT patent number format for U.S.
                 applications updated
NEWS 17 MAR 31
                 LPCI now available as a replacement to LDPCI
NEWS 18 MAR 31
                 EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS 19 APR 04
                 STN AnaVist, Version 1, to be discontinued
NEWS 20 APR 15 WPIDS, WPINDEX, and WPIX enhanced with new
                 predefined hit display formats
NEWS 21 APR 28 EMBASE Controlled Term thesaurus enhanced
NEWS 22 APR 28
                 IMSRESEARCH reloaded with enhancements
NEWS 23 MAY 30
                 INPAFAMDB now available on STN for patent family
                 searching
NEWS 24
         MAY 30
                 DGENE, PCTGEN, and USGENE enhanced with new homology
                 sequence search option
NEWS 25
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                 EPFULL enhanced with 260,000 English abstracts
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         JUN 06
                 KOREAPAT updated with 41,000 documents
NEWS 27
         JUN 13
                 USPATFULL and USPAT2 updated with 11-character
                 patent numbers for U.S. applications
NEWS 28
         JUN 19
                 CAS REGISTRY includes selected substances from
                 web-based collections
NEWS 29
         JUN 25 CA/CAplus and USPAT databases updated with IPC
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reclassification data

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=> s carvedilol
          1943 CARVEDILOL
             1 CARVEDILOLS
L1
          1943 CARVEDILOL
                 (CARVEDILOL OR CARVEDILOLS)
=> s 11 and process for the preparation
       2646810 PROCESS
       1809331 PROCESSES
       3948295 PROCESS
                 (PROCESS OR PROCESSES)
       1620414 PREPARATION
        83372 PREPARATIONS
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                (PROCESS (2W) PREPARATION)
L2
            30 L1 AND PROCESS FOR THE PREPARATION
=> s 12 and organic acid
        414983 ORGANIC
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       1084845 ORG
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       4626919 ACID
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L3
=> s 12 and organic solvent
        414983 ORGANIC
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4035 ORGANICS

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(ORG OR ORGS) 1207500 ORGANIC (ORGANIC OR ORG) 745892 SOLVENT 358054 SOLVENTS 930966 SOLVENT (SOLVENT OR SOLVENTS) 158616 ORGANIC SOLVENT (ORGANIC(W)SOLVENT) L44 L2 AND ORGANIC SOLVENT \Rightarrow s 12 and salts 649684 SALTS 9 L2 AND SALTS L_5 => s 12 and oxalic acid 52412 OXALIC 1 OXALICS 52413 OXALIC (OXALIC OR OXALICS) 4626919 ACID 1640422 ACIDS 5141676 ACID (ACID OR ACIDS) 48958 OXALIC ACID (OXALIC(W)ACID) 3 L2 AND OXALIC ACID L6 => s 12 and salicylic acid 44003 SALICYLIC 2 SALICYLICS 44004 SALICYLIC (SALICYLIC OR SALICYLICS) 4626919 ACID 1640422 ACIDS 5141676 ACID (ACID OR ACIDS) 42236 SALICYLIC ACID (SALICYLIC(W)ACID) L7 2 L2 AND SALICYLIC ACID => s 12 and sslts of carvedilol 0 SSLTS 1943 CARVEDILOL 1 CARVEDILOLS 1943 CARVEDILOL (CARVEDILOL OR CARVEDILOLS) O SSLTS OF CARVEDILOL (SSLTS(1W)CARVEDILOL) 0 L2 AND SSLTS OF CARVEDILOL L8 => s 12 and salts of carvedilol 649684 SALTS 1943 CARVEDILOL 1 CARVEDILOLS 1943 CARVEDILOL (CARVEDILOL OR CARVEDILOLS)

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                 (SALTS (1W) CARVEDILOL)
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             1 L2 AND SALTS OF CARVEDILOL
=> s 12 and crystalline
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           270 CRYSTALLINES
         86439 CRYSTALLINE
                (CRYSTALLINE OR CRYSTALLINES)
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L10
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       1735442 FORM
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L11
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     (FILE 'HOME' ENTERED AT 08:39:55 ON 16 JUL 2008)
     FILE 'HCAPLUS' ENTERED AT 08:40:06 ON 16 JUL 2008
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L4 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:
                         2008:411850 HCAPLUS
                         148:403079
DOCUMENT NUMBER:
TITLE:
                         Process for preparation of
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carvedilol from 4-hydroxycarbazole,

epichlorohydrin, and 2-(2-methoxyphenoxy)ethylamine.

INVENTOR(S): Suri, Sanjay; Kashyap, Tapan

PATENT ASSIGNEE(S): Morepen Laboratories Limited, India

SOURCE: PCT Int. Appl., 21pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| | | ENT | | | | | | | | | | | | | | | ATE | | |
|---|---|----------------|--------|-----|-----|-----|-----|------|-------|-----|------|--------|-----------|----------|-------|------|--------|------------|-----------|
| | | 2008 | | | | | | | | | | | | | | | 0070 | 905 | |
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L4 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:1288806 HCAPLUS

DOCUMENT NUMBER: 144:22811

TITLE: A novel process for the preparation

of 1-(9H-carbazol-4-yloxy)-3-[[2-(-methoxyphenoxy)-

ethyl] amino]-propan-2-ol (carvedilol)

INVENTOR(S): Tarur, Venkatasubramanian Radhakrishnan; Sathe,

Dhananjay Govind; Kulkarni, Swapnil Jayant

PATENT ASSIGNEE(S): USV Limited, India SOURCE: PCT Int. Appl., 14 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

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WO 2005115981
                          Α2
                                20051208
                                          WO 2005-IN139
                                                                   20050503
     WO 2005115981
                          А3
                                20060119
            AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
             LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
             NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL,
             SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA,
             ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
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             RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
             MR, NE, SN, TD, TG
     IN 2004MU00479
                                20060616
                                            IN 2004-MU479
                                                                   20040422
                          Α
     US 20070191456
                                20070816
                                            US 2006-568732
                                                                   20061227
                          A 1
PRIORITY APPLN. INFO.:
                                            IN 2004-MU479
                                                                A 20040422
                                                                W 20050503
                                            WO 2005-IN139
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OTHER SOURCE(S): CASREACT 144:22811

GΙ

AB This invention disclosed a novel process for preparation of carvedilol (I) in high purity by using eco friendly solvents. The process comprised reacting 4-hydroxycarbazole with epichlorhydrin in presence of an organic solvent and a base at temps. between 10° and 30°, and then reacting the resultant 4-(2,3-epoxypropoxy)carbazole with a salt of 2-(2-methoxyphenoxy)ethylamine, preferably the hydrochloride salt, in presence of a base and a hydroxylic solvent at temps. between 30° and 90°.

Ι

L4 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:1154673 HCAPLUS

DOCUMENT NUMBER: 142:93675

TITLE: A process for preparation of 1-[9H-carbazol-4-yloxy]-3-[[2-(2-

methoxyphenoxy)ethyl]amino]propan-2-ol

INVENTOR(S): Chhabada, Vijay Chhangamal; Rehani, Rajeev Budhdev;

Thennati, Rajamannar

PATENT ASSIGNEE(S): Sun Pharmaceutical Industries Limited, India

SOURCE: PCT Int. Appl., 27 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

| PA | ATENT I | NO. | | | KIN | D | DATE | | | APPL | ICAT | ION : | NO. | | | ATE | |
|---------|---------|--------|--------|-----|-----|------|------|------|--------------|----------|-------|----------|------|-----|-----|------|-----|
| WC | 2004 | 1132 | 96 | | A1 | _ | 2004 | | • | WO 2 | 004- | IN52 | | | | | |
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| | | CN, | CO, | CR, | CU, | CZ, | DE, | DK, | DM, | DZ, | EC, | EE, | EG, | ES, | FΙ, | GB, | GD, |
| | | GE, | GH, | GM, | HR, | HU, | ID, | IL, | IN, | IS, | JP, | ΚE, | KG, | KP, | KR, | KΖ, | LC, |
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| | | ΤJ, | TM, | TN, | TR, | TT, | TZ, | UA, | UG, | US, | UZ, | VC, | VN, | YU, | ZA, | ZM, | ZW |
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| | | ES, | FΙ, | FR, | GB, | GR, | HU, | IE, | IT, | LU, | MC, | NL, | PL, | PT, | RO, | SE, | SI, |
| | | SK, | TR, | BF, | ВJ, | CF, | CG, | CI, | CM, | GΑ, | GN, | GQ, | GW, | ML, | MR, | ΝE, | SN, |
| | | TD, | TG | | | | | | | | | | | | | | |
| 11 | N 2003I | O O UM | 647 | | A | | 2005 | 0211 | | IN 2 | 003-1 | MU64 | 7 | | 2 | 0030 | 620 |
| US | S 2006 | 0270 | 858 | | A1 | | 2006 | 1130 | | US 2 | 005- | 5539 | 57 | | 2 | 0051 | 019 |
| PRIORIT | TY APP | LN. | INFO | . : | | | | | | IN 2 | 003-1 | MU64 | 7 | | A 2 | 0030 | 620 |
| | | | | | | | | | | IN 2 | 003-1 | MU72 | 1 | | A 2 | 0030 | 717 |
| | | | | | | | | | | WO 2 | 004- | IN52 | | | W 2 | 0040 | 304 |
| OTHER S | SOURCE | (S): | | | CAS | REAC | T 14 | 2:93 | 675 ; | MAR | PAT | 142: | 9367 | 5 | | | |

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AΒ The present invention provides a process for preparation of 1-[9H-carbazol-4-yloxy]-3-[[2-(2-methoxyphenoxy)ethyl]amino]-propan-2-ol(I) in racemic form or in the form of optically active R or S enantiomer or its pharmaceutically acceptable salt, comprising, reacting 4-(oxiranylmethoxy)-9H-carbazole (II) or the R or S enantiomer thereof with a compound of formula (III) (wherein R1 = benzyl or substituted benzyl), in an aprotic organic solvent in presence of a catalyst to obtain a compound of formula (IV) (wherein R1 is as defined above), or the R or S enantiomer thereof. The resultant compound IV is subjected to debenzylation reaction by catalytic hydrogenation to obtain the compound I, if desired converting the resultant compound I to a pharmaceutically acceptable salt thereof. Thus, to 400 mL EtOAc, 70 q (0.27 mol) anhydrous N-[2-[2-(methoxy)phenoxy]ethyl]benzylamine, 10.25 g (0.075 mol) anhydrous ZnCl2, and 50 g (0.21 mol) 4-(oxiranylmethoxy)-9Hcarbazole were added and the reaction mixture was heated to $70-75^{\circ}$ for 3 h (TLC control for checking conversion to N-benzylcarvedilol), cooled to ambient temperature, and quenched into 100 mL 12-15% aqueous NH3. The aqueous

layer was separated, and the product enriched organic layer was washed with water $\ensuremath{\mathsf{water}}$

till neutral Ph, treated with charcoal, and filtered. To this solution of N-benzyl carvedilol in EtOAc, 7 g wet 5% Pd/C catalyst (50% moisture content) was added and the reaction mixture was hydrogenated at $3.5-4.5~\rm Kg/cm2$ at temperature $60-70^{\circ}$ for a period of about 10 h and filtered. The filtrate was concentrated to remove EtOAc. To the resultant syrupy mass n-butanol (100 mL) was added and the solution was stirred for .apprx.10 h. The crystals were separated by filtration, washed successively with n-butanol (50 mL) and toluene (50 mL) to obtain carvedilol (47 g) which was recrystd. from 3 vols. EtOAc to obtain carvedilol

(42 g).REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2008 ACS on STN 2004:927171 HCAPLUS ACCESSION NUMBER: DOCUMENT NUMBER: 141:395415 TITLE: Process for the preparation of crystalline carvedilol form-II INVENTOR(S): Ramanjaneyulu, Gorantla Seeta; Kumar, Indukuri Venkata Sunil; Rao, Ketavarapu Narasimha; Kishore, Jammula Vera Venkata Krishna PATENT ASSIGNEE(S): Matrix Laboratories Ltd., India PCT Int. Appl., 18 pp. SOURCE: CODEN: PIXXD2 DOCUMENT TYPE: Patent LANGUAGE: English FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION: DATE APPLICATION NO. PATENT NO. KIND DATE _____ ____ A1 20041104 WO 2004-IN104 WO 2004094378 20040416 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG A 20070518 IN 2003-MA328 A1 20060118 EP 2004-727971 IN 2003MA00328 Α 20030421 EP 1615888 20040416 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR A1 20070308 US 2005-552843 US 20070055069 20051012 IN 2003-MA328 PRIORITY APPLN. INFO.: A 20030421 WO 2004-IN104 W 20040416 OTHER SOURCE(S): CASREACT 141:395415 The present invention provides a cost-effective, industrially feasible process for the manufacture of crystalline carvedilol form-II using novel carvedilol salts comprising a step of reacting 4-(2,3-epoxypropoxy) carbazole with 2-(2-methoxyphenoxy) ethylamine followed by acidification with mineral acid in presence of an organic solvent to yield acid addition salts, (e.g. carvedilol oxalate), treatment of the said salts with base(s) in presence of

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REFERENCE COUNT:

organic solvent(s), water, and isolation from the

4

organic solvent(s) followed by crystallization from Et acetate.

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2008:824932 HCAPLUS TITLE: Carvedilol compositions

INVENTOR(S): Patil, Atul Vishvanath; Vishwanathan, Narayanan Badri;

Bhushan, Indu; Reddy, Gade Srinivas; Reddy, Mallepalli

Srinivas; Reddy, Kasaraddy Padmaja

PATENT ASSIGNEE(S): Dr. Reddy's Laboratories Limited, India; Dr. Reddy's

Laboratories, Inc.

SOURCE: PCT Int. Appl., 64pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PAT | ENT | NO. | | | KIN | D | DATE | | | APPL | ICAT | ION : | NO. | | D. | ATE | |
|-------|------|----------|--------|-----|-----|-----|------|------|-----|----------|----------|----------|---------|-----|-----|------|---------|
| WO | 2008 | 0831 | 30 | | A2 | _ | 2008 | 0710 | | WO 2 | 007- | US88 | 774 | | 2 | 0071 | 224 |
| | W: | ΑE, | AG, | AL, | ΑM, | ΑT, | ΑU, | ΑZ, | BA, | BB, | BG, | BH, | BR, | BW, | BY, | BZ, | CA, |
| | | CH, | CN, | CO, | CR, | CU, | CZ, | DE, | DK, | DM, | DO, | DZ, | EC, | EE, | EG, | ES, | FI, |
| | | GB, | GD, | GE, | GH, | GM, | GT, | HN, | HR, | HU, | ID, | IL, | IN, | IS, | JP, | ΚE, | KG, |
| | | KM, | KN, | KP, | KR, | KΖ, | LA, | LC, | LK, | LR, | LS, | LT, | LU, | LY, | MA, | MD, | ME, |
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| | | GH, | GM, | KΕ, | LS, | MW, | MZ, | NΑ, | SD, | SL, | SZ, | TZ, | UG, | ZM, | ZW, | AM, | ΑZ, |
| | | BY, | KG, | KΖ, | MD, | RU, | ТJ, | TM | | | | | | | | | |
| DRITY | APP | LN. | INFO | . : | | | | | | IN 2 | 006- | CH24 | 24 | | A 2 | 0061 | 226 |

PRIORITY APPLN. INFO.: IN 2006-CH2424

US 2007-894712P P 20070314 IN 2007-CH1279 A 20070620

AB Amorphous carvedilol or its pharmaceutically acceptable

salts, their processes of preparation and

pharmaceutical compns. An aspect of the invention relates to amorphous carvedilol phosphate, processes of preparation, and its pharmaceutical compns.

L5 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2008:639197 HCAPLUS

DOCUMENT NUMBER: 148:593035

TITLE: Programmable drug delivery technology

INVENTOR(S): Singh, Amarjit; Singh, Sarabjit; Puthli, Shivanand;

Tandale, Rajendra

PATENT ASSIGNEE(S): Panacea Biotec Limited, India

SOURCE: PCT Int. Appl., 50pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

| PATENT NO. | KIND DATE | APPLICATION NO. | DATE |
|----------------|-----------------|-------------------------|-------------|
| | | | |
| WO 2008062440 | A2 20080529 | WO 2007-IN392 | 20070903 |
| W: AE, AG, AL, | AM, AT, AU, AZ, | BA, BB, BG, BH, BR, BW, | BY, BZ, CA, |

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              IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF,
              BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW,
              GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
              BY, KG, KZ, MD, RU, TJ, TM
                                               IN 2006-MU1411
PRIORITY APPLN. INFO.:
                                                                  A 20060904
     The present invention is concerned with a system for spatially and
     temporally programmable delivery of an active agent. When administered
     orally, the system can be retained in the gastric region for a prolonged
     period of time. It comprises a core, one or more layers coated over the
     core and a preformed hollow space. The invention also concerns with a
     process for preparation of the system and a method for
     treating/preventing diseases, by administering to a subject in need
     thereof, the system of the invention.
     ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:
                          2007:963587 HCAPLUS
DOCUMENT NUMBER:
                          147:308201
                          Novel buccoadhesive compositions comprising a polymer
TITLE:
                          and a sugar and process of
                          preparation thereof
INVENTOR(S):
                          Jain, Rajesh; Jindal, Kour Chand; Devarajan, Sampath
                          Kumar
PATENT ASSIGNEE(S):
                          Panacea Biotec Ltd., India
                          PCT Int. Appl., 45pp.
SOURCE:
                          CODEN: PIXXD2
DOCUMENT TYPE:
                          Patent
LANGUAGE:
                          English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
     PATENT NO.
                         KIND DATE APPLICATION NO. DATE
                         ____
     WO 2007096906
                          A2 20070830
                                            WO 2007-IN74
     WO 2007096906
                          A3
                                20071018
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
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              GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN,
              KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK,
              MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO,
              RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT,
              TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.:

IN 2006-DE512
     Novel buccoadhesive compns. comprising at least one bioactive agent(s), at
     least one bioadhesive polymer(s), at least one water soluble sugar
```

component(s) and at least one binder(s), optionally with other excipients

are provided, wherein the said composition has improved cohesiveness, enhanced intactness and improved adhesion at the desired site of the mucosa for substantially longer duration and releases the bioactive agent(s) in a sustained manner in the oral cavity for extended time period. The composition releases the bioactive agent(s) in the oral cavity such that the bioactive agent is absorbed through the mucosal tissues of the oral cavity thereby bypassing the hepatic metabolism and resulting in increased bioavailability. The bioactive agent(s) is a pharmaceutically active agent(s) or a nutritional supplement(s) or a food product(s), or combinations thereof. Also provided is a process of preparation of such novel compns. comprising steps of (i) mixing the bioactive agent(s) or bioactive agent(s) complexed with cyclodextrin with filler(s); buccoadhesive polymer(s), binder(s), sweetener(s), sugar, color and flavor, optionally with other excipients, (ii) mixing the contents in step (i) with one part of lubricant(s) and roller compacting the blend to obtain compacts, (iii) crushing the compacts/slugs and passing the compacts through suitable sieve to obtain granules, (iv) mixing the granules with the remaining part of lubricant(s) optionally with other excipients, and (v) optionally compressing the blend of step (iv) into a suitable compressed dosage form. Thus, a tablet was prepared containing ondansetron/hydroxypropyl β -cyclodextrin complex 24.36 mg (equivalent to 8 mg of ondansetron base), sodium CM-cellulose (Blanose 7H4XF) 15.00 mg, Plasdone S 630 5.00 mg, maltodextrin 10.00 mg, sucrose 13.16 mg, aspartame 1.00 mg, sodium stearyl fumarate 0.70 mg, Lake of erythrosine 0.07 mg, and strawberry flavor 0.70

L5 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:770875 HCAPLUS

DOCUMENT NUMBER: 148:545974

TITLE: A novel cost effective process for production of

carvedilol phosphate

INVENTOR(S): Shankar, Sanganbhatla; Pandurang, Suryavanshi

Jitendra; Sayyed, Zahid Alam

PATENT ASSIGNEE(S): Wanbury Limited, India SOURCE: Indian Pat. Appl., 13pp.

CODEN: INXXBQ

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|----------|
| | | | | |
| IN 2007MU00929 | A | 20070706 | IN 2007-MU929 | 20070517 |
| PRIORITY APPLN. INFO.: | | | IN 2007-MU929 | 20070517 |

AB A novel cost effective process for the synthesis of phosphate salts of 1-(9H-carbazol-4yloxy)-3-[[2-(2-methoxyphenoxy)ethyl] amino]-propan-2-ol,(carvedilol phosphate) of formula (II) with high yields and purity is disclosed. More particularly, the invention discloses a process of preparation of crystalline phosphate salts of carvedilol using various phosphonation reagents such as phosphorous pentoxide, polyphosphoric acid, Dipotassium hydrogen phosphate, Ammonium Dihydrogen ortho phosphate, and Sodium Dihydrogen ortho phosphate in solvents selected from Acetonitrile, acetone and THF. The solvents used to prepare solvates of carvedilol dihydrogen phosphate are methanol, ethanol and iso-Pr alc.

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ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2008 ACS on STN
L_5
ACCESSION NUMBER: 2004:927171 HCAPLUS
DOCUMENT NUMBER:
                      141:395415
                      Process for the preparation of
TITLE:
                      crystalline carvedilol form-II
                      Ramanjaneyulu, Gorantla Seeta; Kumar, Indukuri Venkata
INVENTOR(S):
                       Sunil; Rao, Ketavarapu Narasimha; Kishore, Jammula
                       Vera Venkata Krishna
PATENT ASSIGNEE(S):
                      Matrix Laboratories Ltd., India
                       PCT Int. Appl., 18 pp.
SOURCE:
                       CODEN: PIXXD2
DOCUMENT TYPE:
                       Patent
LANGUAGE:
                       English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:
                   KIND DATE
    PATENT NO.
                                       APPLICATION NO.
    _____
                                        _____
    WO 2004094378
                      A1 20041104 WO 2004-IN104
       20040416
            TD, TG
                       A 20070518 IN 2003-MA328
A1 20060118 EP 2004-727971
    IN 2003MA00328
                                                              20030421
                       Α
    EP 1615888
                                                              20040416
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR
                    A1 20070308 US 2005-552843
    US 20070055069
                                                             20051012
                                        IN 2003-MA328 A 20030421 WO 2004-IN104 W 20040416
PRIORITY APPLN. INFO.:
                                        WO 2004-IN104
                                                         W 20040416
OTHER SOURCE(S):
                 CASREACT 141:395415
    The present invention provides a cost-effective, industrially feasible
    process for the manufacture of crystalline carvedilol form-II using novel
    carvedilol salts comprising a step of reacting
    4-(2,3-\text{epoxypropoxy}) carbazole with 2-(2-\text{methoxyphenoxy}) ethylamine followed
    by acidification with mineral acid in presence of an organic solvent to yield
    acid addition salts, (e.g. carvedilol oxalate), treatment
    of the said salts with base(s) in presence of organic solvent(s),
    water, and isolation from the organic solvent(s) followed by crystallization
from Et
    acetate.
REFERENCE COUNT:
                       4
                            THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
                            RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
    ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:
                       2004:412919 HCAPLUS
DOCUMENT NUMBER:
                       140:406735
TITLE:
                       Process for the preparation of
```

carvedilol from 4-(oxirane-2-ylmethoxy)-9H-carbazole and 2-(2-methoxyphenoxy)ethylamine

salts

INVENTOR(S): Hercek, Richard; Skoda, Alojz; Proksa, Bohumil

PATENT ASSIGNEE(S): Zentiva, A.S., Slovakia SOURCE: PCT Int. Appl., 13 pp. CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PA | TENT | NO. | | | KIN | D | DATE | | | APPL | ICAT | ION 1 | 7O. | | Di | ATE | | |
|---------|-------|------|------|-----|-----|-----|------|------|-----|------|------|----------|-----------------|-----|-----|------|-----|----|
| WO | 2004 | 0417 | 83 | | A1 | | 2004 | 0521 | | WO 2 | 003- | SK20 | | | 2 | 0031 | 104 | |
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| | | GM, | HR, | HU, | ID, | IL, | IN, | IS, | JP, | ΚE, | KG, | KP, | KR, | KΖ, | LC, | LK, | LR, | |
| | | LS, | LT, | LU, | LV, | MA, | MD, | MG, | MK, | MN, | MW, | MX, | MZ, | NΙ, | NO, | NΖ, | OM, | |
| | | PG, | PH, | PL, | PT, | RO, | RU, | SC, | SD, | SE, | SG, | SK, | SL, | SY, | ΤJ, | TM, | TN, | |
| | | TR, | TT, | TZ, | UA, | UG, | US, | UZ, | VC, | VN, | YU, | ZA, | ZM, | ZW | | | | |
| | RW: | BW, | GH, | GM, | KE, | LS, | MW, | MZ, | SD, | SL, | SZ, | TZ, | UG, | ZM, | ZW, | AM, | ΑZ, | |
| | | BY, | KG, | KΖ, | MD, | RU, | ТJ, | TM, | ΑT, | BE, | ВG, | CH, | CY, | CZ, | DE, | DK, | EE, | |
| | | ES, | FΙ, | FR, | GB, | GR, | HU, | ΙE, | ΙT, | LU, | MC, | ΝL, | PT, | RO, | SE, | SI, | SK, | |
| | | TR, | BF, | ΒJ, | CF, | CG, | CI, | CM, | GΑ, | GN, | GQ, | GW, | ML , | MR, | ΝE, | SN, | TD, | ΤG |
| SK | 2855 | 47 | | | В6 | | 2007 | 0301 | | SK 2 | 002- | 1595 | | | 2 | 0021 | 108 | |
| AU | 2003 | 3018 | 61 | | A1 | | 2004 | 0607 | | AU 2 | 003- | 3018 | 61 | | 2 | 0031 | 104 | |
| EP | 1558 | 575 | | | A1 | | 2005 | 0803 | | EP 2 | 003- | 8107 | 32 | | 2 | 0031 | 104 | |
| | R: | ΑT, | BE, | CH, | DE, | DK, | ES, | FR, | GB, | GR, | ΙT, | LI, | LU, | NL, | SE, | MC, | PT, | |
| | | ΙE, | SI, | LT, | LV, | FI, | RO, | MK, | CY, | AL, | TR, | BG, | CZ, | EE, | HU, | SK | | |
| US | 2006 | 0167 | 077 | | A1 | | 2006 | 0727 | | US 2 | 005- | 5338 | 09 | | 2 | 0050 | 505 | |
| PRIORIT | Y APP | LN. | INFO | .: | | | | | | SK 2 | 002- | 1595 | | | A 2 | 0021 | 108 | |
| | | | | | | | | | | WO 2 | 003- | SK20 | | 1 | W 2 | 0031 | 104 | |

OTHER SOURCE(S): CASREACT 140:406735

AB Carvedilol is prepared in high yield and selectivity by the reaction of 4-(oxirane-2-ylmethoxy)-9H-carbazole with acid-addition salts of 2-(2-methoxyphenoxy)ethylamine [e.g., 2-(2-methoxyphenoxy)ethylamine hydrochloride] in the presence of a base (e.g., potassium carbonate) in an C2-5 alc. solvent (e.g., isopropanol) at an elevated temperature (e.g., 83°).

L5 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:282536 HCAPLUS

DOCUMENT NUMBER: 138:292802

TITLE: Pseudopolymorphic forms of carvedilol

INVENTOR(S): Bubendorf, Andre Gerard; Gabel, Rolf-dieter; Henning,

Michael; Krimmer, Siegfried; Neugebauer, Guenter;

Preis, Walter; Wirl, Alexander F. Hoffmann-La Roche Ag, Switz.

PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag SOURCE: PCT Int. Appl., 35 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PARTILI ACC. NOM. COUNT.

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| | | | | |
| WO 2003029214 | A1 | 20030410 | WO 2002-EP10451 | 20020918 |

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            LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
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            UA, UG, UZ, VN, YU, ZA, ZM, ZW
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            FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
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                              20030410
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                             20041013
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    US 20030119893
                      A1
                               20030626
                                           US 2002-255290
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    MX 2004PA02826
                               20040702
                                          MX 2004-PA2826
                                                                  20040325
                       B1 20070830
A1 20041007
    KR 752549
                                          KR 2004-704578
                                                                  20040327
                                                                  20040420
    US 20040198812
                                           US 2004-827859
                         A1
    US 20060148878
                               20060706
                                           US 2006-325754
                                                                  20060105
PRIORITY APPLN. INFO.:
                                           EP 2001-123422
                                                             A 20010928
                                           WO 2002-EP10451
                                                             W 20020918
                                           US 2002-255290
                                                              B1 20020926
                                           US 2004-827859
                                                               B1 20040420
AB
    The present invention is related to pseudopolymorphic forms of
    1-(4-carbazolyloxy)-3[2-(2-methoxyphenoxy)ethylamino]-2-propanol (
    carvedilol) or its optically active forms or pharmaceutically
    acceptable salts, processes for their prepn
     ., and pharmaceutical compns. containing them for the treatment or prophylaxis
    of cardiac diseases.
REFERENCE COUNT:
                              THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
                              RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
    ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2008 ACS on STN
                        1999:96212 HCAPLUS
ACCESSION NUMBER:
DOCUMENT NUMBER:
                        130:158418
TITLE:
                        Thermodynamically stable modification of
                        1-(4-carbazolyloxy)-3-[2-(2-methoxyphenoxy)ethylamino]-
                        2-propanol, process for its
                        preparation and pharmaceutical compositions
                        containing it
INVENTOR(S):
                        Reinholz, Erhard; Beyer, Peter
PATENT ASSIGNEE(S):
                        Boehringer Mannheim G.m.b.H., Germany
                        PCT Int. Appl., 20 pp.
SOURCE:
                        CODEN: PIXXD2
DOCUMENT TYPE:
                        Patent
LANGUAGE:
                        English
FAMILY ACC. NUM. COUNT: 2
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PATENT INFORMATION:

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KIND DATE APPLICATION NO. DATE
    PATENT NO.
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           LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL,
            PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US,
            UZ, VN, YU, ZW
        RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
           FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
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               A1 19990127 EP 1997-112491
    EP 893440
       R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
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                A1 19990204
               C 20051115
A 19990216
B2 20011101
A1 20000517
B1 20030402
                                       CA 1998-2296637
                                                             19980718
    CA 2296637
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    AU 740453
    EP 1000027
                                       EP 1998-937576
                                                              19980718
    EP 1000027
       R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
   IE, SI, LT, LV, FI, RO
                                                             19980718
                                                             19980718
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                                                            19980718
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                                                            19980718
                                                             20000113
                                                             20000121
                                                             20010102
                                                             20020610
                                       EP 1997-112491 A 19970722
WO 1998-EP4475 W 19980718
US 2000-463346 B1 20000121
PRIORITY APPLN. INFO.:
    The present invention relates to a new thermodynamically stable
AB
    modification of Carvedilol, pharmacol. acceptable salts
    , or optically active forms thereof, processes for the
    preparation, and pharmaceutical compns. containing it. Crude
    carvedilol is heated with MeOH and CXA-coal to give forms I and II
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carvedilol is heated with MeOH and CXA-coal to give forms I and II and these are recrystd. in isopropanol to give pure form I.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2008 ACS on STN ACCESSION NUMBER: 1999:90419 HCAPLUS

DOCUMENT NUMBER: 130:144175

TITLE: Thermodynamically stable modification of

carvedilol, process for its

preparation and pharmaceutical compositions

containing it

INVENTOR(S): Beyer, Peter; Reinholz, Erhard PATENT ASSIGNEE(S): Boehringer Mannheim GmbH, Germany

SOURCE: Eur. Pat. Appl., 11 pp. CODEN: EPXXDW

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

| PA: | TENT I | | | | KINI | | DATE | | | APE | PLIC | CAT | ION 1 | | | | ATE | |
|------------------|----------------|--------------|----------|-----|----------------|------|------------------|------|-----|-------|-------|----------|--------------|-----|-----|-----|--------------|-----|
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| CA | 19981 | MA01. 637 | | шт, | LV, A A1 | | 2005 1999 | 0204 | | | | | MA15 | | | | 9980 9980 | |
| | 22960 99051 | | | | C A1 | | 2005 1999 | | | TAT (| 100 | 30 | EP44 | 75 | | 1 | 9980 | 710 |
| WO | 9903. ₩: | | ΔM | ΔТ | | | BA, | | | | | | | | CN | | | |
| | VV • | | | | | | GE, | | | | | | | | | | | |
| | | | | | | | LU, | | | | | | | | | | | |
| | | | | | | | SG, | | | | | | | | | | | |
| | | UΖ, | VN, | YU, | ZW | · | · | · | • | | • | · | , | · | • | · | , | · |
| | RW: | GH, | GM, | KE, | LS, | MW, | SD, | SZ, | UG, | ZV | V , Z | ΑT, | BE, | CH, | CY, | DE, | DK, | ES, |
| | | FI, | FR, | GB, | GR, | ΙE, | ΙΤ, | LU, | MC, | NI | , E | ₽Τ, | SE, | BF, | ВJ, | CF, | CG, | CI, |
| | | CM, | GΑ, | GN, | GW, | ML, | MR, | NE, | SN, | ΤI |), [| ΓG | | | | | | |
| AU | 98863 | 319 | | | А | | 1999 | 0216 | | AU | 199 | 98- | 8631 | 9 | | 1 | 9980 | 718 |
| | 7404 | | | | В2 | | 2001 | | | | | | | | | | | |
| | 10000 | | | | A1 | | 2000 | | | ΕP | 199 | 98- | 9375 | 76 | | 1 | 9980 | 718 |
| EP | 10000 | | | | В1 | | 2003 | | | | | | | | | | | |
| | R: | | | | | | ES, | FR, | GB, | GF | ₹, - | IT, | LI, | LU, | NL, | SE, | MC, | PT, |
| TD | 2000 | | | LI, | LV, | F.T. | | 0701 | | TT D | 200 | 2.0 | 1.40 | | | 1 | 0000 | 710 |
| | 20000 | | 8 | | T2 | | 2000 | | | | | | 148 | c | | | 9980 | |
| | 9810 | | 0.0 | | A A2 | | 2000 | | | | | | 1077 3198 | | | | 9980 9980 | |
| | 20000 | | 90 98 | | | | 2001 | | | пО | 200 | J U – | 2130 | | | 1 | 2200 | /10 |
| | 2001! | | 24 | | A3 T | | 2001 | | | TP | 200 |) N – | 5041 | 0.4 | | 1 | 9980 | 718 |
| | 50213 | | | | Ā | | 2002 | | | | | | 5021 | | | | 9980 | |
| | 50563 | | | | В | | 2002 | | | | | | 8711 | | | | 9980 | |
| | 23612 | | | | Τ | | 2003 | 0415 | | ΑT | 199 | 98- | 9375 | 76 | | 1 | 9980 | 718 |
| RU | 2202 | 542 | | | C2 | | 2003 | 0420 | | RU | 200 | O 0 C | 1030 | 33 | | 1 | 9980 | 718 |
| PT | 10000 | 027 | | | T | | 2003 | 0731 | | РΤ | 199 | 98- | 9375 | 76 | | 1 | 9980 | 718 |
| CN | 11250 | 047 | | | В | | 2003 | 1022 | | CN | 199 | 98- | 8074 | 36 | | 1 | 9980 | 718 |
| ES | 21953 | 366 | | | Т3 | | 2003 | 1201 | | ES | 199 | 98- | 9375 | 76 | | 1 | 9980 | 718 |
| IL | 1336 | 77 | | | Α | | 2004 | 0601 | | IL | 199 | 98- | 1336 | 77 | | 1 | 9980 | 718 |
| | 1916 | | | | В1 | | 2006 | | | | | | 3384 | 32 | | | 9980 | |
| | 2969 | | | | В6 | | 2006 | | | | | | 221 | | | | 9980 | |
| | 9806 | | _ | | A | | 2000 | | | | | | 6475 | | | | 9980 | |
| | 20000 | | | | A | | 2000 | | | | | | 507 | | | | 0000 | _ |
| | 20000 | | UΙ | | A D1 | | 2000 | | | NO | 200 | JU- | 301 | | | 2 | 0000 | 121 |
| | 31358 | | | | B1 A1 | | 2002 2004 | | | עוו | 200 | 1 | 1000 | 1 2 | | 2 | 0010 | 102 |
| | 2003 | | 550 | | A1 | | 2004 | | | | | | 1661 | | | | 0010 0020 | |
| | 67303 | | J J J | | B2 | | 2003 | | | υD | 200 | J Z = | 1001 | 00 | | ۷ | 0020 | 010 |
| PRIORIT | | | TNFO | . • | ے د | | 200 1 | 0004 | | ЕP | 190 | 97- | 1124 | 91 | | д 1 | 9970 | 722 |
| _ I_ \\I\ I I . | | | -14L O | • • | | | | | | | | | EP44 | | | | 9980 | |
| | | | | | | | | | | | | | | . • | | | | 0 |

US 2000-463346 B1 20000121

AB A new thermodynamically stable modification of 1-(4-carbazolyloxy)-3-[2-(2-methoxyphenoxy)ethylamino]-2-propanol (carvedilol), pharmacol. acceptable salts, or optically active forms thereof, processes for the preparation, and pharmaceutical compns. containing it is disclosed. Thus, 300 g crude carvedilol, 15 g CXA-coal and 2800 methanol was heated for 15 min under reflux, then the hot solution was filtered, washed with 300 mL hot methanol and heated under reflux again. Subsequently the solution was cooled down to 0° and the product was isolated, washed with methanol and dried to obtain 203-255 g of pure form I. Form II can be obtained by addnl. recrystn. process in isopropanol.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L6 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2008:411850 HCAPLUS

DOCUMENT NUMBER: 148:403079

TITLE: Process for preparation of

carvedilol from 4-hydroxycarbazole,

epichlorohydrin, and 2-(2-methoxyphenoxy)ethylamine.

INVENTOR(S):
Suri, Sanjay; Kashyap, Tapan

PATENT ASSIGNEE(S): Morepen Laboratories Limited, India

SOURCE: PCT Int. Appl., 21pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| | 2008 | U303 | ∩1 | | 7\1 | _ | 2009 | 0403 | , | | | | | | 2 | 0070 | 905 |
|--------|-------|------|--------|-------|------|------|------|-------|------|------|------|-------|-------|------|------|------|-----|
| WO | | | | | | | | | | | | | | | | | |
| | W: | • | • | • | • | • | AU, | • | • | • | • | • | • | • | • | • | , |
| | | CH, | CN, | CO, | CR, | CU, | CZ, | DE, | DK, | DM, | DO, | DZ, | EC, | EE, | EG, | ES, | ĿΊ, |
| | | GB, | GD, | GE, | GH, | GM, | GT, | HN, | HR, | HU, | ID, | IL, | IN, | IS, | JP, | KΕ, | KG, |
| | | KM, | KN, | KP, | KR, | KΖ, | LA, | LC, | LK, | LR, | LS, | LT, | LU, | LY, | MA, | MD, | ME, |
| | | MG, | MK, | MN, | MW, | MX, | MY, | MZ, | NA, | NG, | NΙ, | NO, | NZ, | OM, | PG, | PH, | PL, |
| | | PT, | RO, | RS, | RU, | SC, | SD, | SE, | SG, | SK, | SL, | SM, | SV, | SY, | ΤJ, | TM, | TN, |
| | | TR, | TT, | TZ, | UA, | UG, | US, | UZ, | VC, | VN, | ZA, | ZM, | ZW | | | | |
| | RW: | ΑT, | BE, | BG, | CH, | CY, | CZ, | DE, | DK, | EE, | ES, | FΙ, | FR, | GB, | GR, | HU, | IE, |
| | | IS, | ΙΤ, | LT, | LU, | LV, | MC, | MT, | NL, | PL, | PT, | RO, | SE, | SI, | SK, | TR, | BF, |
| | | ВJ, | CF, | CG, | CI, | CM, | GΑ, | GN, | GQ, | GW, | ML, | MR, | NE, | SN, | TD, | TG, | BW, |
| | | GH, | GM, | ΚE, | LS, | MW, | MZ, | NA, | SD, | SL, | SZ, | TZ, | UG, | ZM, | ZW, | AM, | AZ, |
| | | BY, | KG, | KΖ, | MD, | RU, | ТJ, | TM | | | | | | | | | |
| IN | 2006 | DE01 | 711 | | Α | | 2008 | 0404 | | IN 2 | 006- | DE17 | 11 | | 2 | 0060 | 926 |
| IORIT | APP | LN. | INFO | . : | | | | | | IN 2 | 006- | DE17 | 11 | 2 | A 2 | 0060 | 926 |
| HER SO | DURCE | (S): | | | CAS | REAC | T 14 | 8:40 | 3079 | | | | | | | | |
| Car | rvedi | 101 | (T) | was i | orep | ared | by · | react | ion | of. | 4-hv | drox. | vcari | hazo | le w | ith | |

AB Carvedilol (I) was prepared by reaction of 4-hydroxycarbazole with epichlorohydrin in an organic solvent in the presence of base, isolation of the intermediate 4-(2,3-epoxypropoxy)carbazole as a solid cake and reaction of this with 2-(2-methoxyphenoxy)ethylamine in an organic solvent. The crude I is converted to pure product either through solvent crystallization (without salt formation) or through salt formation followed by salt

cleavage and solvent crystallization

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:1154673 HCAPLUS

DOCUMENT NUMBER: 142:93675

TITLE: A process for preparation of

1-[9H-carbazol-4-yloxy]-3-[[2-(2-

methoxyphenoxy)ethyl]amino]propan-2-ol

INVENTOR(S): Chhabada, Vijay Chhangamal; Rehani, Rajeev Budhdev;

Thennati, Rajamannar

PATENT ASSIGNEE(S): Sun Pharmaceutical Industries Limited, India

SOURCE: PCT Int. Appl., 27 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PA' | TENT 1 | NO. | | | KIN | D | DATE | | | APPL | ICAT | ION : | NO. | | | ATE | |
|----------|--------|----------|--------|-----|-----|------|------|------|--------------|----------|-------|----------|------|-----|-----|------|-----|
| WO | 2004 | 1132 | 96 | | A1 | _ | 2004 | | • | WO 2 | 004- | IN52 | | | | | |
| | W: | ΑE, | AG, | AL, | ΑM, | ΑT, | ΑU, | ΑZ, | BA, | BB, | BG, | BR, | BW, | BY, | BZ, | CA, | CH, |
| | | CN, | CO, | CR, | CU, | CZ, | DE, | DK, | DM, | DZ, | EC, | EE, | EG, | ES, | FΙ, | GB, | GD, |
| | | GE, | GH, | GM, | HR, | HU, | ID, | IL, | IN, | IS, | JP, | ΚE, | KG, | KP, | KR, | KΖ, | LC, |
| | | LK, | LR, | LS, | LT, | LU, | LV, | MA, | MD, | MG, | MK, | MN, | MW, | MX, | MΖ, | NA, | ΝI, |
| | | NO, | NZ, | OM, | PG, | PH, | PL, | PT, | RO, | RU, | SC, | SD, | SE, | SG, | SK, | SL, | SY, |
| | | ТJ, | TM, | TN, | TR, | TT, | TZ, | UA, | UG, | US, | UZ, | VC, | VN, | YU, | ZA, | ZM, | ZW |
| | RW: | BW, | GH, | GM, | ΚE, | LS, | MW, | MZ, | SD, | SL, | SZ, | TZ, | UG, | ZM, | ZW, | AM, | ΑZ, |
| | | BY, | KG, | KΖ, | MD, | RU, | ТJ, | TM, | AT, | BE, | BG, | CH, | CY, | CZ, | DE, | DK, | EE, |
| | | ES, | FI, | FR, | GB, | GR, | HU, | IE, | IT, | LU, | MC, | NL, | PL, | PT, | RO, | SE, | SI, |
| | | SK, | TR, | BF, | ВJ, | CF, | CG, | CI, | CM, | GA, | GN, | GQ, | GW, | ML, | MR, | NE, | SN, |
| | | TD, | TG | | | | | | | | | | | | | | |
| IN | 20031 | 0 0 UM | 647 | | A | | 2005 | 0211 | | IN 2 | 003-1 | MU64 | 7 | | 2 | 0030 | 620 |
| US | 2006 | 0270 | 858 | | A1 | | 2006 | 1130 | | US 2 | 005- | 5539 | 57 | | 2 | 0051 | 019 |
| PRIORIT | Y APP | LN. | INFO | .: | | | | | | IN 2 | 003-1 | MU64 | 7 | | A 2 | 0030 | 620 |
| | | | | | | | | | | IN 2 | 003-1 | MU72 | 1 | | A 2 | 0030 | 717 |
| | | | | | | | | | | WO 2 | 004- | IN52 | | | W 2 | 0040 | 304 |
| OTHER SO | OURCE | (S): | | | CAS | REAC | T 14 | 2:93 | 675 ; | MAR | PAT | 142: | 9367 | 5 | | | |

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention provides a process for preparation of 1-[9H-carbazol-4-yloxy]-3-[[2-(2-methoxyphenoxy)ethyl]amino]-propan-2-ol (I) in racemic form or in the form of optically active R or S enantiomer or its pharmaceutically acceptable salt, comprising, reacting 4-(oxiranylmethoxy)-9H-carbazole (II) or the R or S enantiomer thereof with a compound of formula (III) (wherein R1 = benzyl or substituted benzyl), in an aprotic organic solvent in presence of a catalyst to obtain a compound of formula (IV) (wherein R1 is as defined above), or the R or S enantiomer thereof. The resultant compound IV is subjected to debenzylation reaction by catalytic hydrogenation to obtain the compound I, if desired

the

converting the resultant compound I to a pharmaceutically acceptable salt thereof. Thus, to 400 mL EtOAc, 70 g (0.27 mol) anhydrous N-[2-[2-(methoxy)phenoxy]ethyl]benzylamine, 10.25 g (0.075 mol) anhydrous ZnCl2, and 50 g (0.21 mol) 4-(oxiranylmethoxy)-9H-carbazole were added and the reaction mixture was heated to 70-75° for 3 h (TLC control for checking conversion to N-benzylcarvedilol), cooled to ambient temperature, and quenched into 100 mL 12-15% aqueous NH3. The aqueous layer was separated, and

product enriched organic layer was washed with water till neutral Ph, treated with charcoal, and filtered. To this solution of N-benzyl carvedilol in EtOAc, 7 g wet 5% Pd/C catalyst (50% moisture content) was added and the reaction mixture was hydrogenated at $3.5-4.5~{\rm Kg/cm2}$ at temperature $60-70^{\circ}$ for a period of about 10 h and filtered. The filtrate was concentrated to remove EtOAc. To the resultant syrupy mass n-butanol (100 mL) was added and the solution was stirred for .apprx.10 h. The crystals were separated by filtration, washed successively with n-butanol (50 mL) and toluene (50 mL) to obtain carvedilol (47 g) which was recrystd. from 3 vols. EtOAc to obtain carvedilol (42 g).

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:927171 HCAPLUS

DOCUMENT NUMBER: 141:395415

TITLE: Process for the preparation of crystalline carvedilol form-II

INVENTOR(S): Ramanjaneyulu, Gorantla Seeta; Kumar, Indukuri Venkata

Sunil; Rao, Ketavarapu Narasimha; Kishore, Jammula

Vera Venkata Krishna

PATENT ASSIGNEE(S): Matrix Laboratories Ltd., India

SOURCE: PCT Int. Appl., 18 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

| PATENT NO. | | | KINI |) | DATE | | - | APPL: | ICAT | ION I | NO. | | D. | ATE | | |
|-------------|-------|-----|------|-----|------|------|-----|-------|-------|-------|-----|-----|-----|------|-----|----|
| WO 2004094 | | | A1 | | 2004 | 1104 | , | WO 2 | 004- | IN10 | 4 | | 2 | 0040 | 416 | |
| W: AE | , AG, | AL, | AM, | AT, | ΑU, | ΑZ, | BA, | BB, | BG, | BR, | BW, | BY, | BZ, | CA, | CH, | |
| CI | , CO, | CR, | CU, | CZ, | DE, | DK, | DM, | DZ, | EC, | EE, | EG, | ES, | FΙ, | GB, | GD, | |
| GE | , GH, | GM, | HR, | HU, | ID, | IL, | IN, | IS, | JP, | ΚE, | KG, | KP, | KR, | KΖ, | LC, | |
| LF | LR, | LS, | LT, | LU, | LV, | MA, | MD, | MG, | MK, | MN, | MW, | MX, | MZ, | NA, | ΝI, | |
| NC | NZ, | OM, | PG, | PH, | PL, | PT, | RO, | RU, | SC, | SD, | SE, | SG, | SK, | SL, | SY, | |
| TJ | , TM, | TN, | TR, | TT, | TZ, | UA, | UG, | US, | UZ, | VC, | VN, | YU, | ZA, | ZM, | ZW | |
| RW: BV | GH, | GM, | ΚE, | LS, | MW, | MZ, | SD, | SL, | SZ, | TZ, | UG, | ZM, | ZW, | AM, | AZ, | |
| B | , KG, | KΖ, | MD, | RU, | ТJ, | TM, | AT, | BE, | BG, | CH, | CY, | CZ, | DE, | DK, | EE, | |
| ES | , FI, | FR, | GB, | GR, | HU, | IE, | ΙΤ, | LU, | MC, | NL, | PL, | PT, | RO, | SE, | SI, | |
| SF | TR, | BF, | ВJ, | CF, | CG, | CI, | CM, | GΑ, | GN, | GQ, | GW, | ML, | MR, | ΝE, | SN, | |
| TI | , TG | | | | | | | | | | | | | | | |
| IN 2003MA0 | 0328 | | Α | | 2007 | 0518 | | IN 2 | 003-1 | MA32 | 8 | | 2 | 0030 | 421 | |
| EP 1615888 | | | A1 | | 2006 | 0118 | | EP 2 | 004- | 7279 | 71 | | 2 | 0040 | 416 | |
| R: Al | , BE, | CH, | DE, | DK, | ES, | FR, | GB, | GR, | ΙΤ, | LI, | LU, | NL, | SE, | MC, | PT, | |
| IE | , SI, | LT, | LV, | FI, | RO, | MK, | CY, | AL, | TR, | BG, | CZ, | EE, | HU, | PL, | SK, | HR |
| US 2007005 | 5069 | | A1 | | 2007 | 0308 | | US 2 | 005- | 5528 | 43 | | 2 | 0051 | 012 | |
| RITY APPLN. | INFO. | . : | | | | | | IN 2 | 003-1 | MA32 | 8 | | A 2 | 0030 | 421 | |

WO 2004-IN104 W 20040416

CASREACT 141:395415 OTHER SOURCE(S):

AB The present invention provides a cost-effective, industrially feasible process for the manufacture of crystalline carvedilol form-II using novel carvedilol salts comprising a step of reacting 4-(2,3-epoxypropoxy) carbazole with 2-(2-methoxyphenoxy) ethylamine followed by acidification with mineral acid in presence of an organic solvent to yield acid addition salts, (e.g. carvedilol oxalate), treatment of the said salts with base(s) in presence of organic solvent(s), water, and isolation from the organic solvent(s) followed by crystallization from Et

acetate.

REFERENCE COUNT: THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L7 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2008:411850 HCAPLUS

DOCUMENT NUMBER: 148:403079

Process for preparation of TITLE:

carvedilol from 4-hydroxycarbazole,

epichlorohydrin, and 2-(2-methoxyphenoxy)ethylamine.

APPLICATION NO.

DATE

Suri, Sanjay; Kashyap, Tapan INVENTOR(S):

PATENT ASSIGNEE(S): Morepen Laboratories Limited, India

SOURCE: PCT Int. Appl., 21pp.

PATENT NO. KIND DATE

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| | | | | | | _ | | | | | | | | | _ | | |
|--------|-------|------|-----|------|------|----------------|------|------|------|------|------|------|------|-----|------|------|--------|
| WO | 2008 | 0383 | 01 | | A1 | | 2008 | 0403 | | WO 2 | 007- | IN38 | 9 | | 2 | 0070 | 905 |
| | W: | ΑE, | AG, | AL, | AM, | ΑT, | ΑU, | ΑZ, | BA, | BB, | BG, | BH, | BR, | BW, | BY, | BZ, | CA, |
| | | CH, | CN, | CO, | CR, | CU, | CZ, | DE, | DK, | DM, | DO, | DZ, | EC, | EE, | EG, | ES, | FI, |
| | | GB, | GD, | GE, | GH, | GM, | GT, | HN, | HR, | HU, | ID, | IL, | IN, | IS, | JP, | KΕ, | KG, |
| | | KM, | KN, | KP, | KR, | KΖ, | LA, | LC, | LK, | LR, | LS, | LT, | LU, | LY, | MA, | MD, | ME, |
| | | MG, | MK, | MN, | MW, | MX, | MY, | MZ, | NA, | NG, | NΙ, | NO, | NΖ, | OM, | PG, | PH, | PL, |
| | | PT, | RO, | RS, | RU, | SC, | SD, | SE, | SG, | SK, | SL, | SM, | SV, | SY, | ΤJ, | TM, | TN, |
| | | TR, | TT, | TZ, | UA, | UG, | US, | UZ, | VC, | VN, | ZA, | ZM, | ZW | | | | |
| | RW: | ΑT, | BE, | ВG, | CH, | CY, | CZ, | DE, | DK, | EE, | ES, | FΙ, | FR, | GB, | GR, | HU, | IE, |
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| | | | | | | | GA, | | | | | | | | | | |
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| | | | | • | | • | ТJ, | | | | | | | | | | |
| | 2006 | | | | А | | 2008 | 0404 | | | | | | | | | |
| IORIT | | | - | | | | | | | IN 2 | 006- | DE17 | 11 | | A 2 | 0060 | 926 |
| HER SC | - | , . | | | | _ | | | | | | | | | | | |
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The crude I is converted to pure product either through solvent crystallization

(without salt formation) or through salt formation followed by salt

cleavage and solvent crystallization

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:927171 HCAPLUS

DOCUMENT NUMBER: 141:395415

TITLE: Process for the preparation of crystalline carvedilol form-II

INVENTOR(S): Ramanjaneyulu, Gorantla Seeta; Kumar, Indukuri Venkata

Sunil; Rao, Ketavarapu Narasimha; Kishore, Jammula

Vera Venkata Krishna

PATENT ASSIGNEE(S): Matrix Laboratories Ltd., India

SOURCE: PCT Int. Appl., 18 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PAT | TENT | NO. | | | KIN | D | DATE | | | | - | ION I | | | D | ATE | | |
|------|---------------------------|-------|------|-----|-----|-----|------|------|-----|------|------|-------|-----|-----|-----|------|-----|----|
| WO | 2004 | 0943 | 78 | | A1 | _ | 2004 | 1104 | | | | | | | 2 | 0040 | 416 | |
| | W: | ΑE, | AG, | AL, | AM, | ΑT, | ΑU, | ΑZ, | BA, | BB, | BG, | BR, | BW, | BY, | BZ, | CA, | CH, | |
| | | CN, | CO, | CR, | CU, | CZ, | DE, | DK, | DM, | DZ, | EC, | EE, | EG, | ES, | FΙ, | GB, | GD, | |
| | | GE, | GH, | GM, | HR, | HU, | ID, | IL, | IN, | IS, | JP, | KΕ, | KG, | KP, | KR, | KΖ, | LC, | |
| | | LK, | LR, | LS, | LT, | LU, | LV, | MA, | MD, | MG, | MK, | MN, | MW, | MX, | MZ, | NA, | NI, | |
| | • • | | | OM, | PG, | PH, | PL, | PT, | RO, | RU, | SC, | SD, | SE, | SG, | SK, | SL, | SY, | |
| | TJ, TM, | | | TN, | TR, | TT, | TZ, | UA, | UG, | US, | UZ, | VC, | VN, | YU, | ZA, | ZM, | ZW | |
| | RW: BW, GH, | | | GM, | KΕ, | LS, | MW, | MZ, | SD, | SL, | SZ, | TZ, | UG, | ZM, | ZW, | AM, | ΑZ, | |
| | RW: BW, GH, BY, KG, | | | KΖ, | MD, | RU, | ТJ, | TM, | ΑT, | BE, | BG, | CH, | CY, | CZ, | DE, | DK, | EE, | |
| | | ES, | FI, | FR, | GB, | GR, | HU, | ΙE, | ΙT, | LU, | MC, | NL, | PL, | PT, | RO, | SE, | SI, | |
| | | SK, | TR, | BF, | ВJ, | CF, | CG, | CI, | CM, | GΑ, | GN, | GQ, | GW, | ML, | MR, | NE, | SN, | |
| | | TD, | ΤG | | | | | | | | | | | | | | | |
| ΙN | 2003 | MA00. | 328 | | Α | | 2007 | 0518 | | IN 2 | 003- | MA32 | 8 | | 2 | 0030 | 421 | |
| EΡ | 1615 | 888 | | | A1 | | 2006 | 0118 | | EP 2 | 004- | 7279 | 71 | | 2 | 0040 | 416 | |
| | R: | ΑT, | BE, | CH, | DE, | DK, | ES, | FR, | GB, | GR, | ΙT, | LI, | LU, | NL, | SE, | MC, | PT, | |
| | R: AT, BE, C IE, SI, L | | | | LV, | FI, | RO, | MK, | CY, | AL, | TR, | BG, | CZ, | EE, | HU, | PL, | SK, | HR |
| US | US 20070055069 | | | | A1 | | 2007 | 0308 | | US 2 | 005- | 5528 | 43 | | 2 | 0051 | 012 | |
|)RIT | Y APP | LN. | INFO | .: | | | | | | IN 2 | 003- | MA32 | 8 | | A 2 | 0030 | 421 | |
| | | | | | | | | | , | WO 2 | 004- | IN10 | 4 | 1 | W 2 | 0040 | 416 | |

OTHER SOURCE(S): CASREACT 141:395415

AB The present invention provides a cost-effective, industrially feasible process for the manufacture of crystalline carvedilol form-II using novel carvedilol salts comprising a step of reacting 4-(2,3-epoxypropoxy)carbazole with 2-(2-methoxyphenoxy)ethylamine followed by acidification with mineral acid in presence of an organic solvent to yield acid addition salts, (e.g. carvedilol oxalate), treatment of the said salts with base(s) in presence of organic solvent(s), water, and isolation from the organic solvent(s) followed by crystallization from Et acetate.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L9 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2008 ACS on STN

10552843

ACCESSION NUMBER: 2007:770875 HCAPLUS

DOCUMENT NUMBER: 148:545974

TITLE: A novel cost effective process for production of

carvedilol phosphate

INVENTOR(S): Shankar, Sanganbhatla; Pandurang, Suryavanshi

Jitendra; Sayyed, Zahid Alam

PATENT ASSIGNEE(S): Wanbury Limited, India SOURCE: Indian Pat. Appl., 13pp.

CODEN: INXXBQ

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|-----------------------------------|-------------|----------------|-------------------------------------|----------------------|
| DDTA | IN 2007MU00929 RITY APPLN. INFO.: | A | 20070706 | IN 2007-MU929 IN 2007-MU929 | 20070517 20070517 |
| | | | <i>c</i> | | |
| AB | A novel cost effect | ive pro | cess for the | e synthesis of phosphate | salts of |
| | 1-(9H-carbazol-4ylo | xy) - 3 - [| [2-(2-methox)] | <pre>xyphenoxy)ethyl] amino]-</pre> | propan-2-ol,(|
| | carvedilol phosphat | e) of f | ormula (II) | with high yields and pu | rity |
| | is disclosed. More | partic | ularly, the | invention discloses a | |
| | process of preparat | ion of | crystalline | phosphate salts of | |
| | carvedilol using va | rious p | hosphonation | reagents such as | |
| | phosphorous pentoxi | de, pol | yphosphoric | acid, Dipotassium hydro | gen |
| | phosphate, Ammonium | Dihydr | ogen ortho p | hosphate, and Sodium Di | hydrogen |
| | ortho phosphate in | solvent | s selected f | rom Acetonitrile, aceto | ne and THF. |
| | The solvents used t | o prepa | re solvates | of carvedilol dihydroge | n |

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L10 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2008 ACS on STN

phosphate are methanol, ethanol and iso-Pr alc.

ACCESSION NUMBER: 2008:832216 HCAPLUS

TITLE: Novel polymorphic forms of carvedilol

dihydrogen phosphate and process for preparing the

same

INVENTOR(S): Jetti, Ramakoteswara Rao; Gorantla, Asha Rani; Tyaqi,

Om Dutt

PATENT ASSIGNEE(S): Matrix Laboratories Limited, India

SOURCE: U.S. Pat. Appl. Publ., 30pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|------------------------|------|----------|-----------------|---|----------|
| | | | | - | |
| US 20080167477 | A1 | 20080710 | US 2007-852213 | | 20070907 |
| PRIORITY APPLN. INFO.: | | | IN 2007-CH46 | Α | 20070108 |
| | | | IN 2007-CH485 | А | 20070309 |

AB The present invention provides novel crystalline polymorphic forms and amorphous form of carvedilol dihydrogen phosphate characterized by different solid state techniques. The novel processes for their preparation are also disclosed.

L10 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:770875 HCAPLUS

DOCUMENT NUMBER: 148:545974

TITLE: A novel cost effective process for production of

carvedilol phosphate

INVENTOR(S): Shankar, Sanganbhatla; Pandurang, Suryavanshi

Jitendra; Sayyed, Zahid Alam

PATENT ASSIGNEE(S): Wanbury Limited, India SOURCE: Indian Pat. Appl., 13pp.

CODEN: INXXBO

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. IN 2007MU00929 _____ A 20070706 IN 2007-MU929 IN 2007-MU929 20070517 PRIORITY APPLN. INFO.: 20070517 A novel cost effective process for the synthesis of phosphate salts of 1-(9H-carbazol-4yloxy)-3-[[2-(2-methoxyphenoxy)ethyl] amino]-propan-2-ol,(carvedilol phosphate) of formula (II) with high yields and purity is disclosed. More particularly, the invention discloses a process of preparation of crystalline phosphate salts of carvedilol using various phosphonation reagents such as phosphorous pentoxide, polyphosphoric acid, Dipotassium hydrogen phosphate, Ammonium Dihydrogen ortho phosphate, and Sodium Dihydrogen ortho phosphate in solvents selected from Acetonitrile, acetone and THF. The solvents used to prepare solvates of carvedilol dihydrogen phosphate are methanol, ethanol and iso-Pr alc.

L10 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:1338211 HCAPLUS

DOCUMENT NUMBER: 146:68735

TITLE: Crystalline forms of carvedilol and processes for their preparation

INVENTOR(S): Lifshitz, Igor; Wizel, Shlomit

PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva

Pharmaceuticals USA, Inc.

SOURCE: PCT Int. Appl., 17pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

| PATENT NO. | KIND DA | ATE APP | LICATION NO. | DATE |
|----------------|------------|----------------|--------------------|-------------|
| | | | | |
| WO 2006135757 | A1 20 | 0061221 WO | 2006-US22499 | 20060609 |
| W: AE, AG, AL, | AM, AT, A | AU, AZ, BA, BE | B, BG, BR, BW, BY, | BZ, CA, CH, |
| CN, CO, CR, | CU, CZ, DI | DE, DK, DM, DZ | I, EC, EE, EG, ES, | FI, GB, GD, |
| GE, GH, GM, | HR, HU, I | ID, IL, IN, IS | S, JP, KE, KG, KM, | KN, KP, KR, |
| KZ, LC, LK, | LR, LS, L | LT, LU, LV, LY | T, MA, MD, MG, MK, | MN, MW, MX, |
| MZ, NA, NG, | NI, NO, N | NZ, OM, PG, PH | I, PL, PT, RO, RU, | SC, SD, SE, |
| SG, SK, SL, | SM, SY, To | IJ, TM, TN, TR | R, TT, TZ, UA, UG, | US, UZ, VC, |
| VN, YU, ZA, | ZM, ZW | | | |

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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
              IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
              CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
              GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
              KG, KZ, MD, RU, TJ, TM
     US 20070043099 A1 20070222 US 2006-450699
EP 1781611 A1 20070509 EP 2006-772705
                                                                         20060609
                                                                        20060609
         R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
              IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL,
              BA, HR, MK, YU
     KR 2007088507 A
                                   20070829
                                               KR 2007-705429
                                                                         20070307
                                                US 2005-689776P P 20050609
PRIORITY APPLN. INFO.:
                                                                    W 20060609
                                                WO 2006-US22499
     This invention relates to a novel crystalline form of
AΒ
     carvedilol, to processes for its preparation, to
     compns. containing it and to its use in medicine. This invention further
     relates to a novel process for preparing crystalline carvedilol
     . Thus, carvedilol 50 g and Et acetate 500 mL were put into
     clean flask, the slurry was heated to temperature higher than 70 °C to
     get full dissoln. The solution was cooled to about 0-5°C. At temperature
     of about 5-10° spontaneous precipitation occurred. The solid substance was
     filtered and washed by Et acetate.
REFERENCE COUNT:
                           11
                                  THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS
                                  RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
L10 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:216797 HCAPLUS
DOCUMENT NUMBER:
                           142:285152
TITLE:
                          New crystalline forms of carvedilol
INVENTOR(S):
                          Zupet, Rok; Grcman, Marija; Smrkolj, Matej
                        Krka, Tovarna Zdravil D.D. Novo Mesto, Slovenia
PATENT ASSIGNEE(S):
                          PCT Int. Appl., 20 pp.
SOURCE:
                           CODEN: PIXXD2
DOCUMENT TYPE:
                          Patent
LANGUAGE:
                           English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:
     PATENT NO. KIND DATE APPLICATION NO. DATE

      WO 2005021504
      A2
      20050310
      WO 2004-SI29

      WO 2005021504
      A3
      20050602

         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
              CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
              GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
              LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
              NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
              TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, CM, TD, TC
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A 20050430 SI 2003-218 20030902 A2 20060531 EP 2004-775682 20040901

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,

IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK

SI 21616 EP 1660451

SN, TD, TG

PRIORITY APPLN. INFO.: SI 2003-218 A 20030902 WO 2004-SI29 W 20040901

AB The present invention relates to new crystalline carvedilol forms VII and IX and to processes for the preparation Particularly, this invention relates to processes of the isolation of carvedilol, using Et acetate as a solvent and preparation of an Et acetate solvate.

L10 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:927171 HCAPLUS

DOCUMENT NUMBER: 141:395415

TITLE: Process for the preparation of crystalline carvedilol form-II

INVENTOR(S): Ramanjaneyulu, Gorantla Seeta; Kumar, Indukuri Venkata

Sunil; Rao, Ketavarapu Narasimha; Kishore, Jammula

Vera Venkata Krishna

PATENT ASSIGNEE(S): Matrix Laboratories Ltd., India

SOURCE: PCT Int. Appl., 18 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PA: | CENT | NO. | | | KIN |) | DATE | | | APPL | ICAT | ION I | NO. | | D. | ATE | | |
|---------|----------------------------|--------|-----|-----|-----|-----|------|------|-----|------|------|----------|-----|-----|-----|------|-----|----|
| WO | 2004 | 0943 | 78 | | A1 | | 2004 | 1104 | 1 | WO 2 | 004- | IN10 | 4 | | 2 | 0040 | 416 | |
| | W: | ΑE, | AG, | AL, | AM, | ΑT, | AU, | ΑZ, | BA, | BB, | BG, | BR, | BW, | BY, | BZ, | CA, | CH, | |
| | | CN, | CO, | CR, | CU, | CZ, | DE, | DK, | DM, | DZ, | EC, | EE, | EG, | ES, | FI, | GB, | GD, | |
| | | GE, | GH, | GM, | HR, | HU, | ID, | IL, | IN, | IS, | JP, | ΚE, | KG, | KP, | KR, | KΖ, | LC, | |
| | | LK, | LR, | LS, | LT, | LU, | LV, | MA, | MD, | MG, | MK, | MN, | MW, | MX, | MZ, | NA, | NI, | |
| | NO, NZ, C TJ, TM, T | | | OM, | PG, | PH, | PL, | PT, | RO, | RU, | SC, | SD, | SE, | SG, | SK, | SL, | SY, | |
| | TJ, TM, T RW: BW, GH, G | | | TN, | TR, | TT, | TZ, | UA, | UG, | US, | UZ, | VC, | VN, | YU, | ZA, | ZM, | ZW | |
| | RW: BW, GH, G | | | GM, | ΚE, | LS, | MW, | MZ, | SD, | SL, | SZ, | TZ, | UG, | ZM, | ZW, | AM, | ΑZ, | |
| | BY, KG, K | | | KΖ, | MD, | RU, | ТJ, | TM, | AT, | ΒE, | ВG, | CH, | CY, | CZ, | DE, | DK, | EE, | |
| | BY, KG, K ES, FI, F | | | FR, | GB, | GR, | HU, | ΙE, | ΙΤ, | LU, | MC, | NL, | PL, | PT, | RO, | SE, | SI, | |
| | | SK, | TR, | BF, | ΒJ, | CF, | CG, | CI, | CM, | GA, | GN, | GQ, | GW, | ML, | MR, | ΝE, | SN, | |
| | | TD, | ΤG | | | | | | | | | | | | | | | |
| IN | 2003 | 0 0 AM | 328 | | Α | | 2007 | 0518 | | IN 2 | 003- | MA32 | 8 | | 2 | 0030 | 421 | |
| EP | 1615 | 888 | | | A1 | | 2006 | 0118 | | EP 2 | 004- | 7279 | 71 | | 2 | 0040 | 416 | |
| | R: | ΑT, | BE, | CH, | DE, | DK, | ES, | FR, | GB, | GR, | ΙT, | LI, | LU, | NL, | SE, | MC, | PT, | |
| | | ΙE, | SI, | LT, | LV, | FI, | RO, | MK, | CY, | AL, | TR, | BG, | CZ, | EE, | HU, | PL, | SK, | HR |
| US | US 20070055069 | | | | A1 | | 2007 | 0308 | 1 | US 2 | 005- | 5528 | 43 | | 2 | 0051 | 012 | |
| PRIORIT | RITY APPLN. INFO.: | | | | | | | | | IN 2 | 003- | MA32 | 8 | | A 2 | 0030 | 421 | |
| | | | | | | | | | 1 | WO 2 | 004- | IN10 | 4 | 1 | W 2 | 0040 | 416 | |

OTHER SOURCE(S): CASREACT 141:395415

AB The present invention provides a cost-effective, industrially feasible process for the manufacture of crystalline carvedilol form-II using novel carvedilol salts comprising a step of reacting 4-(2,3-epoxypropoxy)carbazole with 2-(2-methoxyphenoxy)ethylamine followed by acidification with mineral acid in presence of an organic solvent to yield acid addition salts, (e.g. carvedilol oxalate), treatment of the said salts with base(s) in presence of organic solvent(s), water, and isolation from the organic solvent(s) followed by crystallization from Et acetate.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:570906 HCAPLUS

DOCUMENT NUMBER: 139:122716

TITLE: Crystalline solids of carvedilol and processes for their preparation

INVENTOR(S): Kor, Ilan; Wizel, Shlomit

PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva

Pharmaceuticals USA, Inc.

SOURCE: PCT Int. Appl., 18 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| | PAT | CENT : | NO. | | | KIN | D | DATE | | | | | | | | D. | ATE | |
|------|------|--------------|--|--|--|--|---|--|--|--|---|--|--|--|--|--|--|--|
| | | 2003 2003 | | | | | | | | | | 003- | | | | 2 | 0030 | 115 |
| | | W: | AE, CO, GM, LS, PL, UA, GH, KG, | AG, CR, HR, LT, PT, UG, GM, KZ, | AL, CU, HU, LU, RO, US, KE, MD, | AM, CZ, ID, LV, RU, UZ, LS, RU, | AT, DE, IL, MA, SC, VC, MW, | AU, DK, IN, MD, SD, VN, MZ, TM, | AZ, DM, IS, MG, SE, YU, SD, AT, | BA, DZ, JP, MK, SG, ZA, SL, BE, | EC, KE, MN, SK, ZM, SZ, BG, | EE, KG, MW, SL, ZW TZ, CH, | ES, KP, MX, TJ, UG, CY, | FI, KR, MZ, TM, ZM, CZ, | GB, KZ, NO, TN, ZW, DE, | GD, LC, NZ, TR, AM, DK, | GE, LK, OM, TT, AZ, EE, | GH, LR, PH, TZ, BY, ES, |
| | | | | | | | | IE, GA, | | | • | | | | • | • | | BF, |
| | CA | 2472 | | | | | | | | | | | | | | | | 115 |
| | | 2003 | | | | | | | | | | | | | | | | |
| | US | 2003 | 0166 | 702 | | A1 | | 2003 | 0904 | | US 2 | 003- | 3429 | 05 | | 2 | 0030 | 115 |
| | US | 6710 | 184 | | | В2 | | 2004 | 0323 | | | | | | | | | |
| | EΡ | 1474 | | | | | | 2004 | | | | | | | | | | |
| | | R: | | | | | | ES, | | | • | | | | • | • | | PT, |
| | | | | | | | | RO, | | | | • | | | | | | |
| | CN | 1615 2005 | 133 | | | А | | 2005 | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | |
| | US | 2004 | 0171 | 665 | | A1 | | 2004 | 0902 | | US 2 | 003- | 7127 | 99 | | 2 | 0031 | 112 |
| | ZA | 2004 | 0054 | 43 | | А | | 2005 | 0708 | | ZA 2 | 004 - | 5443 | | | 2 | 0040 | 708 |
| | MX | 2004 | PA06 | | | | | | | | MX 2 | 004 - 1 | PA69 | | | | | |
| | ИО | 2004 | 0033 | 83 | | Α | | 2004 | 0813 | | NO 2 | 004 - | 3383 | | | 2 | 0040 | 813 |
| PRIO | RITY | APP | LN. | INFO | .: | | | | | | US 2 | 002- | 3493 | 10P |] | P 2 | 0020 | 115 |
| | | | | | | | | | | | | 003- | | | | | | |
| | | | | | | | | | | | WO 2 | 0.03 - 1 | US11 | 37 | 1 | W 2 | 0030 | 115 |
| AB | Thi | is in | vent | ion · | rela: | tes : | to a | nov | el ci | rvst | alli | ne s | olid | of | | | | |

AB This invention relates to a novel crystalline solid of carvedilol or a solvate thereof, to processes for its preparation, to compns. containing it and to its use in medicine. This invention further relates to a novel process for preparing a crystalline solid of carvedilol form II.

=> d l11 ibib abs hitstr tot

L11 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2008 ACS on STN ACCESSION NUMBER: 2004:927171 HCAPLUS

141:395415 DOCUMENT NUMBER:

Process for the preparation of TITLE:

crystalline carvedilol form

INVENTOR(S): Ramanjaneyulu, Gorantla Seeta; Kumar, Indukuri Venkata

Sunil; Rao, Ketavarapu Narasimha; Kishore, Jammula

Vera Venkata Krishna

PATENT ASSIGNEE(S): Matrix Laboratories Ltd., India

SOURCE: PCT Int. Appl., 18 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PA | TENT | NO. | | | KIN |) | DATE | | | APPL | | | | | D | ATE | | |
|-------|------------------------|------|--------|------|------|------|------|------|------|------|------|------|-------|------|------|------|-----|----|
| WO | 2004 | 0943 | 78 | | A1 | | 2004 | 1104 | | | | | | | 2 | 0040 | 416 | |
| | W: | ΑE, | AG, | AL, | AM, | ΑT, | ΑU, | AZ, | BA, | BB, | BG, | BR, | BW, | BY, | BZ, | CA, | CH, | |
| | | CN, | CO, | CR, | CU, | CZ, | DE, | DK, | DM, | DZ, | EC, | EE, | EG, | ES, | FI, | GB, | GD, | |
| | | GE, | GH, | GM, | HR, | HU, | ID, | IL, | IN, | IS, | JP, | KE, | KG, | KP, | KR, | KΖ, | LC, | |
| | | LK, | LR, | LS, | LT, | LU, | LV, | MA, | MD, | MG, | MK, | MN, | MW, | MX, | MZ, | NA, | NI, | |
| | | NO, | NZ, | OM, | PG, | PH, | PL, | PT, | RO, | RU, | SC, | SD, | SE, | SG, | SK, | SL, | SY, | |
| | TJ, TM, RW: BW, GH, | | | | TR, | TT, | TZ, | UA, | UG, | US, | UΖ, | VC, | VN, | YU, | ZA, | ZM, | ZW | |
| | RW: BW, GH, | | | | KE, | LS, | MW, | MΖ, | SD, | SL, | SZ, | TZ, | UG, | ZM, | ZW, | AM, | AZ, | |
| | BY, KG, | | | | MD, | RU, | ТJ, | TM, | ΑT, | BE, | BG, | CH, | CY, | CZ, | DE, | DK, | EE, | |
| | | ES, | FΙ, | FR, | GB, | GR, | HU, | ΙE, | ΙΤ, | LU, | MC, | NL, | PL, | PT, | RO, | SE, | SI, | |
| | | SK, | TR, | BF, | ВJ, | CF, | CG, | CI, | CM, | GΑ, | GN, | GQ, | GW, | ML, | MR, | ΝE, | SN, | |
| | | TD, | ΤG | | | | | | | | | | | | | | | |
| IN | 2003 | MA00 | 328 | | A | | 2007 | 0518 | | IN 2 | 003- | MA32 | 8 | | 2 | 0030 | 421 | |
| EP | 1615 | 888 | | | A1 | | 2006 | 0118 | | EP 2 | 004- | 7279 | 71 | | 2 | 0040 | 416 | |
| | R: | ΑT, | BE, | CH, | DE, | DK, | ES, | FR, | GB, | GR, | ΙT, | LI, | LU, | NL, | SE, | MC, | PT, | |
| | | IE, | SI, | LT, | LV, | FΙ, | RO, | MK, | CY, | AL, | TR, | BG, | CZ, | EE, | HU, | PL, | SK, | HF |
| US | 2007 | 0055 | 069 | | A1 | | 2007 | 0308 | | US 2 | 005- | 5528 | 43 | | 2 | 0051 | 012 | |
| IORIT | Y APP | LN. | INFO | .: | | | | | | IN 2 | 003- | MA32 | 8 | | A 2 | 0030 | 421 | |
| | | | | | | | | WO 2 | 004- | IN10 | 4 | , | W 2 | 0040 | 416 | | | |
| HER S | OURCE | (S): | | | CASI | REAC | T 14 | 1:39 | | | | | | | | | | |
| Th | e pre | sent | inv | enti | on p | rovi | des | a co | st-e | ffec | tive | , in | dust: | rial | ly f | easi | ble | |
| pr | ocess | for | the | man | ufac | ture | of | crvs | tall | ine | carv | edil | 01 | | _ | | | |

process for the manufacture of crystalline carvedilol

form-II using novel carvedilol salts

comprising a step of reacting 4-(2,3-epoxypropoxy) carbazole with 2-(2-methoxyphenoxy)ethylamine followed by acidification with mineral acid in presence of an organic solvent to yield acid addition salts, (e.g. carvedilol oxalate), treatment of the said salts with base(s) in

presence of organic solvent(s), water, and isolation from the organic solvent(s)

followed by crystallization from Et acetate.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:570906 HCAPLUS

DOCUMENT NUMBER: 139:122716

TITLE: Crystalline solids of carvedilol and processes for their preparation

Kor, Ilan; Wizel, Shlomit INVENTOR(S):

PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.

SOURCE: PCT Int. Appl., 18 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| P. | ATENT | NO. | | | | | DATE | | | APPL | | | | | | ATE | |
|----------------------|--|--|--|--|--|--|--|--|--|---------------------------------|--------------------------------|---------------------------------|--------------------------|--------------------------|--------------------------|---------------------------------|--------------------------|
| | 2003 2003 | 0598 | 07 | | A2 | | | | | | | | | | | 0030 | 115 |
| | W: | AE, CO, GM, LS, PL, UA, | AG, CR, HR, LT, PT, UG, | AL, CU, HU, LU, RO, US, | AM, CZ, ID, LV, RU, UZ, | AT, DE, IL, MA, SC, VC, | AU, DK, IN, MD, SD, VN, | AZ, DM, IS, MG, SE, YU, | BA, DZ, JP, MK, SG, ZA, | EC, KE, MN, SK, ZM, | EE, KG, MW, SL, ZW | ES, KP, MX, TJ, | FI, KR, MZ, TM, | GB, KZ, NO, TN, | GD, LC, NZ, TR, | CH, GE, LK, OM, TT, | GH, LR, PH, TZ, |
| C | A 2472 | KG, FI, BJ, | KZ, FR, CF, | MD, GB, CG, | RU, GR, CI, | TJ, HU, CM, | TM, IE, GA, | AT, IT, GN, | BE, LU, GQ, | BG, MC, GW, | CH, NL, ML, | CY, PT, MR, | CZ, SE, NE, | DE, SI, SN, | DK, SK, TD, | EE, TR, TG | ES, BF, |
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| EI | R: | 133 AT, | BE, | CH, | A2 DE, | DK, | 2004 | 1110 FR, | GB, | GR, | ΙΤ, | LI, | LU, | NL, | SE, | 0030: MC, SK | |
| JE US ZA MX | 1615 2005 2004 2004 2004 2004 | 5152 0171 0054 PA06 | 26 665 43 909 | | A1 A A | | 2005 2004 2005 2005 | 0526 0902 0708 0419 | | JP 2 US 2 ZA 2 MX 2 | 003- 003- 004- 004- | 5599: 7127: 5443 PA69: | 22 99 09 | | 2 2 2 2 | | 115 112 708 715 |
| PRIORIT | TY APP | LN. | INFO | .: | | | | | | US 2 | 002 003 003- | 3493 3429 US11 | 10P 05 37 | | P 2 A3 2 | 0020: 0030: 0030: | 115 115 |

AB This invention relates to a novel crystalline solid of carvedilol or a solvate thereof, to processes for its preparation, to compns. containing it and to its use in medicine. This invention further relates to a novel process for preparing a crystalline solid of carvedilol form II.

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L12 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:570906 HCAPLUS

DOCUMENT NUMBER: 139:122716

TITLE: Crystalline solids of carvedilol and

processes for their preparation

INVENTOR(S): Kor, Ilan; Wizel, Shlomit

PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva

Pharmaceuticals USA, Inc.

SOURCE: PCT Int. Appl., 18 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| | PATENT NO. WO 2003059807 | | | | | | | | | | ICAT | | | | | ATE | | |
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| | W: | ΑE, | AG, | AL, | AM, | ΑT, | ΑU, | ΑZ, | BA, | BB, | BG, | BR, | BY, | BZ, | CA, | CH, | CN, | |
| | | CO, | CR, | CU, | CZ, | DE, | DK, | DM, | DZ, | EC, | EE, | ES, | FΙ, | GB, | GD, | GE, | GH, | |
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| | | LS, | LT, | LU, | LV, | MA, | MD, | MG, | MK, | MN, | MW, | MX, | MZ, | NO, | NZ, | OM, | PH, | |
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| | | UA, | UG, | US, | UZ, | VC, | VN, | YU, | ZA, | ZM, | ZW | | | | | | | |
| | RW: | GH, | GM, | ΚE, | LS, | MW, | MΖ, | SD, | SL, | SZ, | TZ, | UG, | ZM, | ZW, | AM, | AZ, | BY, | |
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| | | ВJ, | CF, | CG, | CI, | CM, | GΑ, | GN, | GQ, | GW, | ML, | MR, | NE, | SN, | TD, | ΤG | | |
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| | 6710 | | | | | | | | | | | | | | | | | |
| EP | 1474 | 133 | | | A2 | | 2004 | 1110 | | EP 2 | 003- | 7038 | 15 | | 2 | 0030 | 115 | |
| | R: | ΑT, | BE, | CH, | DE, | DK, | ES, | FR, | GB, | GR, | ΙΤ, | LI, | LU, | NL, | SE, | MC, | PT, | |
| | | | | | | | | MK, | | | | | | | | | | |
| | 1615 | 133 | | | А | | 2005 | 0511 | 1 | CN 2 | 003- | 8022 | 10 | | 2 | 0030 | 115 | |
| | 2005 | | | | | | | | | | | | | | | | | |
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| | 2004 | | | | | | | | | MX 2 | 004- | PA69 | 09 | | 2 | 0040 | 715 | |
| | 2004 | | | | А | | 2004 | 0813 | | | 004- | | | | | | | |
| IORIT | Y APP | LN. | INFO | .: | | | | | | | 002- | | | | | | | |
| | | | | | | | | | | | 003- | | | | | | | |
| Trib. | | | | _ | | | | _ | | | 003- | | - | | | | | |

AB This invention relates to a novel crystalline solid of carvedilol or a solvate thereof, to processes for its preparation, to compns. containing it and to its use in medicine. This invention further relates to a novel process for preparing a crystalline solid of carvedilol form II.

L12 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:282536 HCAPLUS

DOCUMENT NUMBER: 138:292802

TITLE: Pseudopolymorphic forms of carvedilol

INVENTOR(S): Bubendorf, Andre Gerard; Gabel, Rolf-dieter; Henning,

Michael; Krimmer, Siegfried; Neugebauer, Guenter;

Preis, Walter; Wirl, Alexander F. Hoffmann-La Roche Ag, Switz.

PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag SOURCE: PCT Int. Appl., 35 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

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            W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
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                  GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
                  LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
                  PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
                  UA, UG, UZ, VN, YU, ZA, ZM, ZW
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                  FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
                  CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
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                                                                                            20020918 <--
                                                         EP 2002-777139
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            R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
      IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

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US 2002-255290 B1 20020926

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PRIORITY APPLN. INFO.:
                                                             US 2002-255290 B1 20020926
US 2004-827859 B1 20040420
       The present invention is related to pseudopolymorphic forms of
       1-(4-carbazolyloxy)-3[2-(2-methoxyphenoxy)ethylamino]-2-propanol (
       carvedilol) or its optically active forms or pharmaceutically
       acceptable salts, processes for their preparation, and
       pharmaceutical compns. containing them for the treatment or prophylaxis of
       cardiac diseases.
                                           THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
REFERENCE COUNT:
                                          RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
L12 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:556143 HCAPLUS
                                 137:125080
DOCUMENT NUMBER:
TITLE:
                                  Process for preparing heterocyclic indene analogs by
                                  cyclocarbonylation at moderate temperatures and
                                  catalyst loading
                                  Scalone, Michelangelo; Zeibig, Thomas Albert
INVENTOR(S):
                              Hoffmann-LaRoche Inc., Switz.
PATENT ASSIGNEE(S):
SOURCE:
                                  U.S. Pat. Appl. Publ., 19 pp.
                                  CODEN: USXXCO
                      Patent
DOCUMENT TYPE:
                                 English
LANGUAGE:
FAMILY ACC. NUM. COUNT: 1
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| PATENT NO. | KIND DATE | APPLICATION NO. | DATE |
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| WO 2002059089 WO 2002059089 | A2 20020801 A3 20021031 | CA 2002-2434408 WO 2002-EP583 | 20020122 < |
| W: AE, AG, AL, CO, CR, CU, GM, HR, HU, | AM, AT, AU, AZ, E CZ, DE, DK, DM, E ID, IL, IN, IS, J | BA, BB, BG, BR, BY, BZ, DZ, EC, EE, ES, FI, GB, IP, KE, KG, KP, KR, KZ, | CA, CH, CN, GD, GE, GH, LC, LK, LR, |
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| RW: GH, GM, KE, CY, DE, DK, | LS, MW, MZ, SD, S ES, FI, FR, GB, G | SL, SZ, TZ, UG, ZM, ZW, SR, IE, IT, LU, MC, NL, GN, GQ, GW, ML, MR, NE, | PT, SE, TR, |
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| US 7169935 PRIORITY APPLN. INFO.: | B2 20070130 | US 2002-54462 | A3 20020122 |
| | reparation heteroc | WO 2002-EP583 080; MARPAT 137:125080 cyclic indene analogs, hydroxycarbazole or N- | |
| 4-hydroxycarbazole, This | involves cyclocar | bonylation followed by | |
| process avoids high REFERENCE COUNT: | 4 THERE ARE 4 | catalyst loadings. CITED REFERENCES AVAI CITATIONS AVAILABLE I | |
| L12 ANSWER 4 OF 6 HCAP ACCESSION NUMBER: DOCUMENT NUMBER: | 2000:383901 HCAF 133:22442 | PLUS | |
| TITLE: INVENTOR(S): | | embination preparations ardiovascular disorders | |
| PATENT ASSIGNEE(S): SOURCE: | | oche AG., Switz. 7 pp. | |
| DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION: | Patent English | | |
| PATENT NO. | KIND DATE | APPLICATION NO. | DATE |
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AΒ
     Pharmaceutical prepns. for the treatment of cardiac and cardiovascular
     disorders such as hypertension, angina pectoris, cardiac insufficiency,
     and illnesses associated therewith contain carvedilol, a
     \beta-blocker with addnl. \alpha1-blocking activity, or a salt thereof
     and hydrochlorothiazide, a diuretic, or a salt thereof as a fixed
     combination of active substances, as well as usual additives. The process
     for production of the combination preparation permits the 2 active substance
     granulates to be pressed to a stable tablet in 1 operation, as follows:
     granulates of the 2 agents, each having a moisture content of 6-20% and a
     bulk d. of 0.1-1.5 g/mL, and the granulate moisture content and bulk d. of
     the 2 granulates differing from one another by \leq 30\%. are combined
     to a press mass which is compressed to a solid dosage form, preferably a
     tablet. Since carvedilol is light sensitive, the dosage form is
     coated with a light-protecting film. At disintegrant contents >5%, the
     coating is applied at an initial spray rate sufficiently low to permit
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formation of a film on the tablet surface under conditions of air supply and temperature which remove the water of the film suspension as rapidly as possible from the tablet surface; after this critical phase of film formation

25.000, hydrochlorothiazide 12.500, sucrose 25.000, lactose-H2O 28.060,

is complete, the spray rate is increased to that conventional for film-coating. Thus, tablets were prepared containing carvedilol

PVP 1.780, crosslinked PVP 20.170, microcryst. cellulose 10.000, highly dispersed SiO2 5.320, and Mg stearate 2.170 mg, and coated with a mixture of Et acrylate/Me acrylate copolymer 2.248, Na citrate 0.308, hydroxypropylmethylcellulose 1.018, Macrogol 0.644, talc 1.624, TiO2 0.950, indigo carmine color lacquer 0.170, polysorbate 80 0.034, and dimethicone 0.004 mg.

L12 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1999:96212 HCAPLUS

DOCUMENT NUMBER: 130:158418

TITLE: Thermodynamically stable modification of

1-(4-carbazolyloxy)-3-[2-(2-methoxyphenoxy)ethylamino]-

2-propanol, process for its

preparation and pharmaceutical compositions

containing it

INVENTOR(S):
Reinholz, Erhard; Beyer, Peter

PATENT ASSIGNEE(S): Boehringer Mannheim G.m.b.H., Germany

SOURCE: PCT Int. Appl., 20 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

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| | Dīaī • | | VN, | | | IV/ITAT | CD | C 7 | IIC | 77 TAT | AT, | DE | СП | CV | DE | DIZ | гc | |
| | LW: | | | | | | | | | | PT, | | | | | | | |
| | | | | | GW, | | | | | | | on, | Dr, | ъо, | Cr, | co, | C_{\perp} , | |
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| CA | 2296 | 637 | | | С | | 2005 | 1115 | | | | | | | | | | |
| | 9886 | | | | Α | | | | | AU 1 | 998- | 8631 | 9 | | 1 | 9980 | 718 | < |
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| | 1000 | | | | A1 | | | | | EP 1 | 998- | 9375 | 76 | | 1 | 9980 | 718 | < |
| EP | 1000 | | | | B1 | | 2003 | | | | | | | | | | | |
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| _ | 5021 | | | | Ā | | 2002 | | | _ | 998- | | - | | | 9980 | | |
| | 2361 | | | | T | | 2003 | 0415 | | AT 1 | 998- | 9375 | 76 | | 1 | 9980 | 718 | < |
| RU | 2202 | 542 | | | C2 | | 2003 | 0420 | | RU 2 | 000- | 1030 | 33 | | 1 | 9980 | 718 | < |
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                                               EP 1997-112491 A 19970722
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PRIORITY APPLN. INFO.:
     The present invention relates to a new thermodynamically stable
     modification of Carvedilol, pharmacol. acceptable salts, or
     optically active forms thereof, processes for the prepn
     ., and pharmaceutical compns. containing it. Crude carvedilol is
     heated with MeOH and CXA-coal to give forms I and II and these are
     recrystd. in isopropanol to give pure form I.
                         3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
REFERENCE COUNT:
                                 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
L12 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:90419 HCAPLUS
DOCUMENT NUMBER:
                           130:144175
                          Thermodynamically stable modification of
TITLE:
                           carvedilol, process for its
                          preparation and pharmaceutical compositions
                           containing it
                      Beyer, Peter; Reinholz, Erhard
Boehringer Mannheim GmbH, Germany
INVENTOR(S):
PATENT ASSIGNEE(S):
                           Eur. Pat. Appl., 11 pp.
SOURCE:
                           CODEN: EPXXDW
                     Patent
DOCUMENT TYPE:
                          English
LANGUAGE:
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:
     PATENT NO. KIND DATE APPLICATION NO. DATE
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              LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL,
              PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US,
              UZ, VN, YU, ZW
          RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
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AB A new thermodynamically stable modification of 1-(4-carbazolyloxy)-3-[2-(2-methoxyphenoxy)ethylamino]-2-propanol (carvedilol), pharmacol. acceptable salts, or optically active forms thereof, processes for the preparation, and pharmaceutical compns. containing it is disclosed. Thus, 300 g crude carvedilol, 15 g CXA-coal and 2800 methanol was heated for 15 min under reflux, then the hot solution was filtered, washed with 300 mL hot methanol and heated under reflux again. Subsequently the solution was cooled down to 0° and the product was isolated, washed with methanol and dried to obtain 203-255 g of pure form I. Form II can be obtained by addnl. recrystn. process in isopropanol.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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| COST IN U.S. DOLLARS | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| FULL ESTIMATED COST | 155.21 | 155.42 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| CA SUBSCRIBER PRICE | -26.40 | -26.40 |

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